U.S. ARMY RESEARCH INSTITUTE OF ENVIRONMENTAL MEDICINE

TECHNICAL REPORT NO. T99-5
DATE February 1999
AD A

SPEECH MOTOR CONTROL AND THE DEVELOPMENT OF ACUTE MOUNTAIN SICKNESS

U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND

REPORT NO T99-5

SPEECH MOTOR CONTROL AND THE DEVELOPMENT OF ACUTE MOUNTAIN SICKNESS

U.S. ARMY RESEARCH INSTITUTE
OF
ENVIRONMENTAL MEDICINE

Natick, Massachusetts
01760-5007

February 1999

The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Army or the Department of Defense.

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRMC Regulation 70-25 on the use of volunteers in research.

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	February 1999	Technical report

4. TITLE AND SUBTITLE
Speech motor control and the development of Acute Mountain Sickness

5. FUNDING NUMBERS

6. AUTHOR(S)
Allen Cymerman, Philip Lieberman, Jesse Hochstadt, Paul B. Rock, Gail E. Butterfield, and Lorna G. Moore

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
U.S. Army Research Institute of Environmental Medicine
Natick, MA 01760-5007

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick
Frederick, MD 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

Disturbances in cognition and speech motor control have been associated with high-altitude exposure and may involve selective hypoxic vulnerability of specific brain areas. Given the cerebral origin of AMS, we hypothesized that speech motor control as determined by voice onset timing (VOT) would be an objective measure of AMS. Fifteen women (24.7 ± 1.8 yrs) were studied at sea level and after 4 and 39 h of simulated exposure to 4,300 m altitude. AMS-C was assessed twice daily using the Environmental Symptoms Questionnaire (ESQ-C). Speech motor control was determined from digitally recorded timing patterns of 60 monosyllabic words, representing three places of articulation (labial, alveolar, and velar) and further categorized as "voiced" or "unvoiced." The times between the initial burst of air at the mouth and the beginning of vocal cord resonance (VOT) were reduced at the labial site with 4 and 39 h of exposure. The minimum timed distance between "voiced" and "unvoiced" consonants (MD) was not affected by altitude. Timing differences between the places of articulation were preserved during altitude exposure. ESQ-C scores obtained at 39 h, but not at 4 h, correlated with MDs derived from two places of articulation: labial and velar. VOT may be a promising new tool to objectively assess the severity of AMS.

14. SUBJECT TERMS
Altitude, Acute Mountain Sickness, Altitude Illness, Speech Production

15. NUMBER OF PAGES

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

USARIEM TECHNICAL REPORT T99-??

SPEECH MOTOR CONTROL AND THE DEVELOPMENT OF ACUTE MOUNTAIN SICKNESS (AMS)

Prepared by

Allen Cymerman, Ph.D., Philip Lieberman, Ph.D., Jesse Hochstadt, B.S.,
Paul B. Rock, D.O., Ph.D., Gail E. Butterfield, Ph.D., and Lorna G. Moore, Ph.D.

U.S. ARMY RESEARCH INSTITUTE
OF
ENVIRONMENTAL MEDICINE

Natick, Massachusetts
01760-5007

Approved for public release
Distribution Unlimited

Technical Report T99-??

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

BACKGROUND

High terrestrial elevations have always been areas of significant military strategic value, whether from an observational and training perspective, a political boundary viewpoint, or as a focal site from which insurgency and counter insurgency elements confront one another. Relatively rapid insertion of military personnel into moderate-to-high mountain areas (1500 - 3000 m) with its lowered oxygen content presents challenges in sustaining optimal military performance and health and exposes all personnel to medical problems that may be mission-threatening and possibly life-threatening. One of the major medical problems to be encountered is Acute Mountain Sickness (AMS). In order to assess the effects of any interventions that may mitigate or prevent AMS, a reliable method of measurement is a prerequisite. Current methods include self-administered questionnaires and medical interview. Both methods are fraught with subjective influences that can and often bias results. What is needed is a simple, objective, physiological method that accurately quantifies the severity of AMS symptoms and thus permits reliable testing of potential AMS interventions.

From the early days of aviation research, investigators have noted that speech production and interpretative phenomena were adversely affected when aviators were acutely exposed to moderate to severe hypoxia. Speech production is a complicated phenomena involving coordination of several brain areas and peripheral muscle control. Before obvious disturbances in speech become evident as occurs with severe hypoxia, it should be possible to detect subtle but consistent changes in speech pattern that are reflective of central neurological disturbances stemming from more moderate hypoxia such as found at high terrestrial elevations. Thus, it may be possible to objectively assess the severity of altitude-related illnesses such as acute mountain sickness and high altitude cerebral edema, and do it from a remote location using radio communication.

ACKNOWLEDGMENTS

The dedicated and professional efforts of MSG Mark Sharp, SSG James Moulton, Mr. Vincent A. Forte, and Ms. Shari Hallas in supporting the collection, analysis and presentation of the data are acknowledged and greatly appreciated.

EXECUTIVE SUMMARY

Acute Mountain Sickness (AMS) is a self-limited symptom complex that occurs in unacclimatized individuals who ascend rapidly to altitudes in excess of 2,000 m. The syndrome is characterized by headache, anorexia, nausea, vomiting, insomnia, lassitude, and malaise. The symptoms usually appear within 24 h of exposure and normally resolve after several days. The incidence and severity increase with elevation with, for example, 50% of exposed individuals developing moderate AMS at 3,700 - 4,300 m. In a small number of individuals, AMS may progress into high altitude cerebral edema (HACE) or high altitude pulmonary edema (HAPE), both of which are life-threatening. Even mild symptoms of AMS and related altitude-induced illnesses can negatively affect military performance, well being, and morale to a sufficient degree to compromise mission goals.

AMS is currently assessed by self-administered questionnaires, such as the Environmental Symptoms and the Lake Louise Questionnaires, coupled with a medical interview. The questionnaires and the medical interview are fraught with subjective influences that can and often bias results. Despite these drawbacks, the questionnaires and interview remain the accepted means to quantify the incidence and severity of AMS and are the standard to which correlative measures are made. What is needed is a simple, objective, physiological method that accurately quantifies the severity of AMS symptoms and thus permits more reliable testing of potential AMS interventions.

The cause of AMS is currently thought to be hypoxia-induced subclinical cerebral edema. Because brain swelling may not occur uniformly in a hypoxic brain and because there may be a selective vulnerability of specific brain areas, resultant symptoms such as disturbances in vision and possibly speech may be affected in subtle but quantifiable ways. Deficits in cognitive and psychomotor performance have long been known to occur at altitudes and, although vision has been well studied, there has been almost no research conducted involving speech production and articulation. Nevertheless, speech production remains one of the most complex psychomotor functions and should degrade with cerebral hypoxia.

Speech patterns are under both conscious and subconscious control and involve a very highly coordinated sequence of contractions of the larynx, pharynx, palate, tongue, lips, and respiratory muscles. These areas are innervated by the hypoglossal, vagal, facial, and phrenic nerves whose nuclei are in the motor cortices. As with all muscular movements, there are also influences from the cerebellum and basal ganglia. Histologic studies of the hypoxic brain indicate that compromised cells in the hippocampus, cerebellum and basal ganglia can lead to memory and motor deficits as well as some aphasia. That motor and cognitive deficits are frequent observations at extreme altitudes, especially in individuals suffering severe AMS or high altitude cerebral edema, suggests involvement of the above cerebral anatomical areas. The question remains as to whether subtle changes can be detected when oxygen levels are not as extreme as they are, for example, on a climb of Mt. Everest.

Articulation can be readily quantified by measuring specific parameters of the acoustic waveforms of particular words. Voice waveforms of selected words representing different areas of

articulation (labial, alveolar, and velar) are, for the most part, specific for the individual and not under conscious control. If changes in speech patterns can be associated with AMS, then an objective method will have been found to assess AMS and the effects of interventional strategies.

The objective of this study was twofold. The first objective was to test the hypothesis that deficits in speech motor control would be evident during a 48-h exposure to 4,300 m simulated altitude. The second objective was to test the hypothesis that Voice Onset Timing (VOT), a measure of speech production, would be affected by the presence of AMS. This study was a component of a larger study testing the hypothesis that pharmacologic attenuation of α-adrenergic activity will alter the "normal" hypoxia-induced physiologic changes associated with acclimatization in female, sea-level residents exposed to 4,300 m elevation. A double-blind, placebo-controlled, crossover design was used to test the effect of oral prazosin, an α-adrenergic blocker, on physiologic parameters indicative of acclimatization during 48 h exposure.

Fifteen volunteers were exposed to a simulated altitude of 4,300 m (P_B =446 mmHg) in a hypobaric chamber for 48 h on 2 occasions (phase 1 and 2), separated by 1 month. Speech motor control was determined from digitally recorded and analyzed timing patterns of 30 different monosyllabic words. The Environmental Symptoms Questionnaire (ESQ) was used to assess AMS. Questionnaire scores closest to the voice recordings were used to determine statistical correlations. Only the data obtained during the first exposure were used in the analysis, regardless of whether the subject was on drug or placebo.

During phase 1, three volunteers withdrew from the study prior to completion of the 48-hour protocol (at ~11,~20, and ~30 h) due to severe AMS. During the crossover phase, 2 of the 3 subjects again withdrew from the study due to severe AMS. AMS severity showed the typical temporal response with measurable symptoms occurring after 4 h, peaking at 16 h, and returning toward sea level after 48 h. Labial VOTs were shorter after 4 and 39 h of exposure; velar VOTs were altered only after 4 h; and there were no changes in alveolar VOTs. The relative relationship between the sites of articulation was not changed by altitude exposure. The duration of vowel sounds was increased after 4 h of exposure and returned to normal thereafter. Only 1 of 15 subjects did not increase vowel time after 4 h of exposure. After 39 h, only 2 of the 12 subjects had vowel times shorter than their initial sea-level values. Significant positive correlations were found between the voiced-unvoiced timed separations of the 39-h labial and velar consonants and the symptoms of AMS. Only a trend was obtained between vowel lengthening and AMS severity (P=0.12).

In summary, two objective measures of speech production, namely specific parameters of VOT and vowel lengthening, were found to be affected by acute exposure to 4,300 m simulated altitude. Minimum timed differences between voiced and unvoiced consonants at the labial and velar places of articulation were positively correlated with the severity of AMS. It appears that speech production is altered in subtle ways by acute exposure to 4,300 m altitude. This alteration is not readily apparent to the subject at this altitude and may be related to selective central vulnerability to hypoxia. Further validation is required before VOT can be used to reliably assess AMS severity, but the method is promising.

INTRODUCTION

ETIOLOGY OF AMS

Acute Mountain Sickness (AMS) is a syndrome that is characterized by headache, anorexia, nausea, vomiting, insomnia, lassitude, and malaise. The syndrome has great individual variation in susceptibility; however, the hypoxia-induced symptoms are most common in unacclimatized low-altitude residents who rapidly ascend to terrestrial elevations exceeding 2,500 m. The symptoms of AMS commonly appear within 4 to 24 h of exposure and usually resolve after several days as acclimatization to hypoxia is achieved. Acute Mountain Sickness is usually self-limited, but may progress into high altitude cerebral edema (HACE) or high altitude pulmonary edema (HAPE), both of which are potentially life-threatening (6,11,14,15).

The most widely accepted hypothesis about the cause of AMS symptoms is that the symptoms are a manifestation of hypoxia-induced, subclinical cerebral edema that causes swelling of the brain ((10,12,26,27). The predominant symptoms used in the cerebral classification of AMS are taken from a subset of questions on the Environmental Symptoms Questionnaire (ESQ) that include 11 items concerned with cerebral or central dysfunction. Items such as lightheadedness, headache, dizziness, etc., are general descriptors and not easily amendable to objective physiological measurement. The severity of headache, the principal symptom of AMS, is most likely reported differently by individuals.

USE OF SPEECH PATTERNS TO ASSESS CEREBRAL DYSFUNCTION

Speech production is a complicated process involving higher cortical centers with cognitive and associative functions, as well as motor control centers for respiration, and muscles of the face, mouth, and throat. Coordinated contractions of the larynx, pharynx, palate, tongue, lips, and respiratory muscles, in addition to the higher cortical functions, are necessary for understandable speech. Deterioration of speech motor control is evident in diseases such as Broca's aphasia and Parkinsonism (2,9,19) and may involve pathways to and from the basal ganglia in addition to the higher cerebral centers. One of the speech attributes that is amenable to analysis is Voice Onset Timing (VOT). From acoustic analyses of specific words, it is possible to quantitate the disruptive nature of specific conditions or situations by measuring specific parameters of the word waveforms. VOT of selected words representing different areas of articulation (labial, alveolar, and velar) are, for the most part, specific for the individual and not under conscious control. VOT and vowel length are not affected by practice or minor fatigue. Voice Onset Timing has been used to study disease manifestations and treatments, speech development, and language differences (3,5,7,13,19,23), but only one investigator has applied the technique to individuals exposed to hypoxic conditions.

Lieberman et al. (20) were the first to apply the technique of VOT to normal individuals exposed to a severe hypoxic environment where cerebral function could be affected. During a climb of Mt. Everest, they found that VOT separations of voiced and unvoiced consonants of five climbers were significantly reduced from base camp (5,300 m) to 7150 m before ascent and after descent. At Camp 2 (6300 m) and Camp 3 (7150 m), the VOT reduction was considered sufficiently reduced for comprehension of voiced and unvoiced consonants to present a problem. The extreme environment

of a Mt. Everest climb presents multiple hazards to the climber such as fatigue, dehydration (especially of the upper airways), and hypothermia. Their results could easily have been affected by any of the above acting synergistically or additively with the ever-present hypoxia, compounding the effects on the brain.

Because of the confounding environmental influences encountered on an actual expedition to high altitude and the possibility that climbers could be suffering from several undiagnosed altitude-related maladies that could affect speech production, a hypobaric chamber study was conducted under simulated conditions to control as many extraneous factors as possible. To date, no attempts have been made to use VOT to study exposure environmental extremes under controlled environmental conditions. If changes in speech patterns can be associated with accompanying AMS, then an objective method will have been found to assess AMS and interventional strategies.

METHODS

SUBJECTS

Fifteen female volunteers participated in the study, with a mean (±S.E.) age of 24.7 ±1.2 yrs, body weight of 70.6 ±2.4 kg, and height of 169.2±2.0 cm. They were all born at elevations below 1,500 m and resided at sea level for 6 months prior to the study. Physical exams and medical histories were considered normal by a physician. Each was fully informed of the nature of the study, gave written consent, and was made aware of the right to withdraw without prejudice at any time.

DESIGN

A double-blind, placebo-controlled, crossover design was used. Following a 66-h sea-level baseline test period, subjects were decompressed at a rate of 45 mmHg•min^{-1} to a terrestrial altitude equivalent of 4,300 m (446 mmHg) and remained at this barometric pressure for the next 48 h. Temperature and relative humidity were maintained at 23±2°C and 55±5% throughout the study. Re-exposure 1 month later utilized the same simulated environmental conditions. In the double-blind, crossover design, subjects received either placebo or 1 mg oral prazosin (Pfizer Labs) every 8 h commencing 66 h before exposure. During the entire testing period, subjects were required to consume a specified quantity of a controlled diet and liquid consisting of a commercial liquid formula, commercial prepared food items, and nonprepared items of known energy and nutritional content.

MEASUREMENTS

AMS symptoms were assessed utilizing the ESQ, which was administered at 0700 and 1900 h during sea-level and altitude testing phases. The ESQ is a self-reported 67-question symptom inventory designed to quantify symptoms induced by altitude and other stressful environments and conditions. To document the severity of AMS, a weighted average of cerebral (ESQ-C) symptoms were calculated from the ESQ scores (25). An ESQ-C value of 0.7 or greater indicated the presence

of AMS. The effectiveness of ESQ-C scores in identifying individuals with AMS has been previously reported and validated (25).

Speech motor control (VOT) was determined from digitally recorded and analyzed timed patterns of a list of 30 English monosyllabic words read twice (Table 1). The voice recordings were obtained using a portable digital tape recorder (Sony Digital Micro Recorder NT-2) at sea level and after 4 and 39 h of exposure. Voice digitization occurred at 32 kHz with 12-bit nonlinear quantization. Recordings were resampled at 20kHz using 12-bit linear quantization and analyzed using proprietary software (BLISS, Brown University). The 30 monosyllabic words represent three places of articulation (labial, alveolar, and velar) and are further categorized as being initiated by a "voiced" or "unvoiced" stop consonant as shown in Table 2. VOT and vowel duration were determined from acoustic landmarks shown in Figure 1. The time between the initial burst of air at the mouth and the beginning of vocal cord resonance (phonation) is defined as the VOT. The vowel duration is determined from the onset of phonation to the end of phonation. Other than a slowly acquired familiarization with the word list, subjects did not practice reading the words. No more than 3 h separated ESQ from VOT measurements.

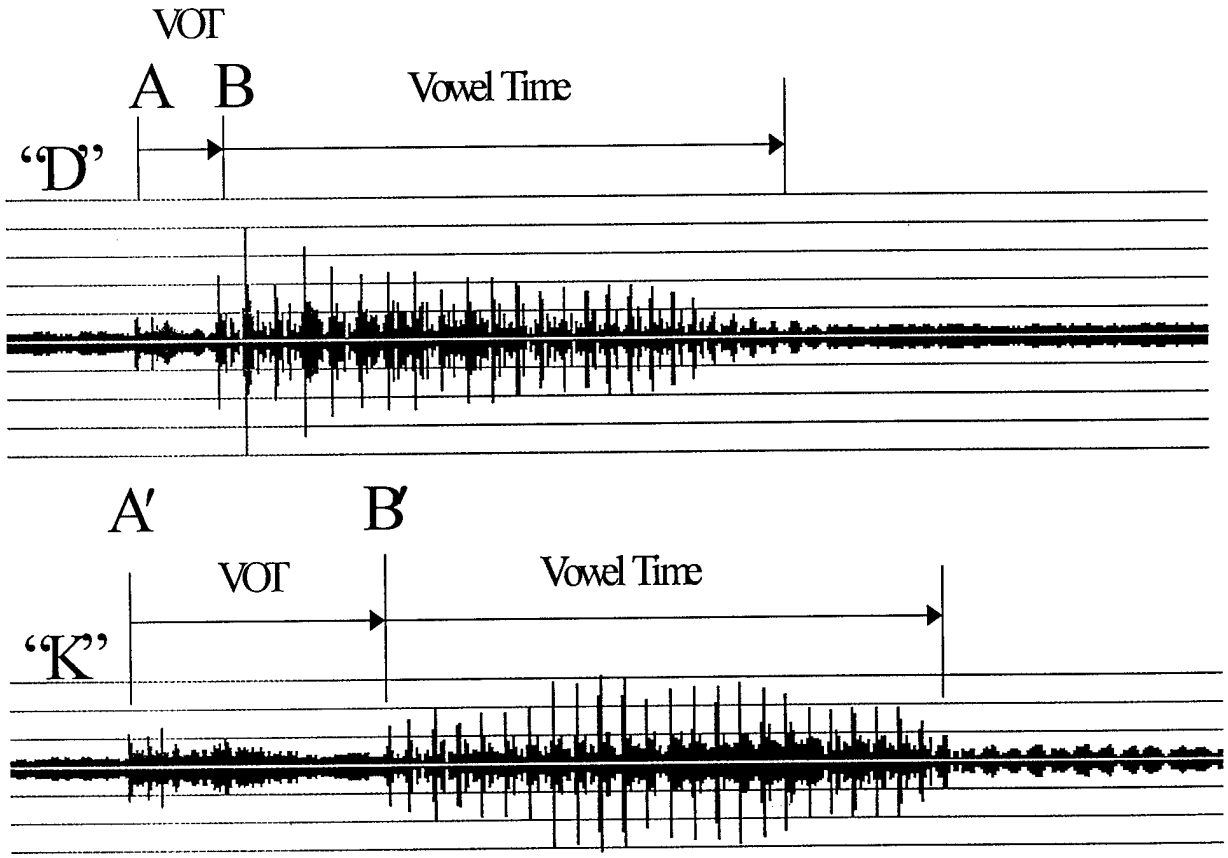
Table 1. List of 30 English monosyllabic words used to determine VOT at three places of articulation (labial, alveolar, and velar).

Instructions: Please read each of the words on the list below as though it were a sentence. Pause between each word. After you finish, read it a second time.	
Bad	Take
Tag	Gab
Keep	Goat
Kid	Cook
Dad	Big
Dab	Tide
Boot	God
Pad	Pat
Top	Took
Cap	Gap
Good	Pig
Dope	Cab
Pick	Dig
Pipe	Bag
Bat	Dip

Table 2. Classification of consonants based upon anatomical location of articulation. Voiced consonants have VOTs characteristically ~20 msec in length, while unvoiced VOT consonants are usually 40 msec or longer. Labial consonants are initiated at the lips; alveolar consonants at the hard palate; and velar consonants at the soft palate.

	LABIAL	ALVEOLAR	VELAR
VOICED	B	D	G
UNVOICED	P	T	K

Figure 1. Sample acoustic waveform patterns for the words "dope" and "kid," corresponding to voiced (D) and unvoiced (K) consonants. VOT is the time (msec) between cursors A and B (25 msec) or A' and B' (98 msec). Vowel duration (msec) is the length of resonance.



ESQ-C scores of phase 1 closest to the voice recordings were used to determine subsequent statistical correlations. Only the data obtained during the first exposure, regardless of whether the subject was on drug or placebo, were used in the analyses.

STATISTICAL ANALYSIS

Values are presented as mean ± standard error (SE) except where noted. Data were analyzed using standard two-way or one-way repeated-measures analysis of variance. Significant main effects were localized using Tukey's least significant difference post hoc test. Tests of possible relationships between variables were performed using the Pearson Product-Moment Correlation method. Statistical significance was accepted at $p \leq 0.05$.

RESULTS

ACUTE MOUNTAIN SICKNESS

Table 3 shows the subject treatment order and illness outcome for phases 1 and 2. Also indicated are subjects who were considered ill with scores 0.7 or higher on the ESQ-C. There was no effect of prazosin on the incidence or severity of AMS (two-way repeated measures ANOVA of treatment (prazosin-placebo) versus time; $F=2.39$, $p=0.15$). A second two-way repeated measures ANOVA of trial versus time ($F=8.15$, $p=0.01$) indicated a significant difference between phase 1 and phase 2. During phase 1 the mean ESQ-C was 0.90 ± 0.07, and during phase 2 the ESQ-C score was 0.64 ± 0.06. As a result, only phase 1 ESQ scores were used in subsequent comparisons with parameters of speech production.

During phase 1, 10 of the 15 subjects had scores above the illness threshold. During this phase, 3 subjects were removed from hypobaric hypoxia due to severe AMS symptoms: subject 1 after 11 h; subject 7 after 30 h; and subject 8 after 20 h. Eight of the remaining 12 were still significantly ill after 39 h. During phase 2, only 7 of the 15 subjects were ill after 4 h, and 4 of 13 after 39 h. Subject 7 was removed from hypobaric hypoxia after 11 h and subject 8 after 19 h of exposure.

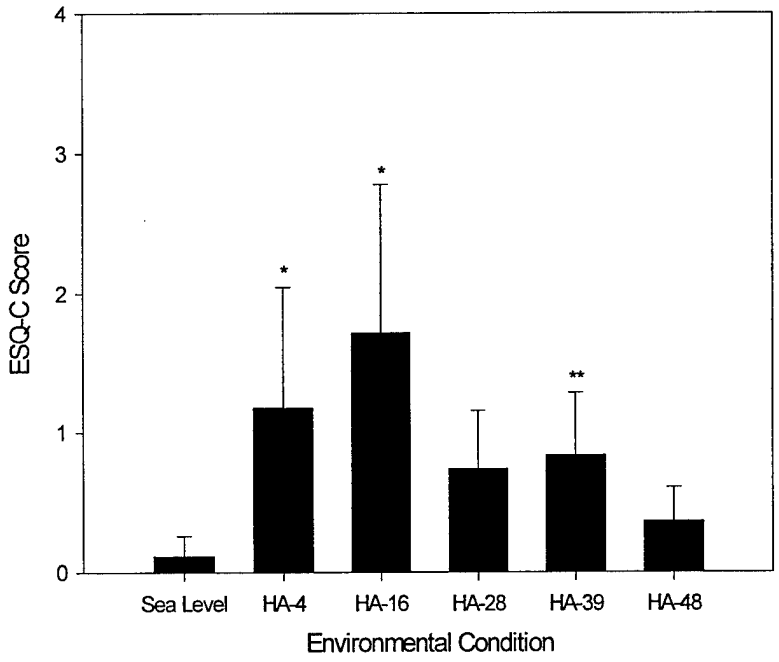
Table 3. Individual subject treatment order and AMS outcome. An ESQ-C of 0.7 or higher was indicative of AMS. Numbers in parentheses indicate length of exposure time prior to removal from the study due to severe AMS symptoms.

	PHASE 1			PHASE 2		
SUBJECT	TREATMENT	AMS*		TREATMENT	AMS*	
		4 hrs	39 hrs		4 hrs	39 hrs
1	Prazosin	Yes	(11)	Placebo	Yes	Yes
2	Placebo	No	Yes	Prazosin	No	No
3	Placebo	No	Yes	Prazosin	No	Yes
4	Placebo	No	No	Prazosin	No	No
5	Prazosin	Yes	Yes	Placebo	No	No
6	Placebo	Yes	No	Prazosin	Yes	No
7	Prazosin	Yes	(30)	Placebo	Yes	(19)
8	Placebo	Yes	(20)	Prazosin	No	(11)
9	Prazosin	Yes	No	Placebo	No	No
10	Prazosin	Yes	Yes	Placebo	Yes	No
11	Placebo	Yes	Yes	Prazosin	Yes	Yes
12	Placebo	Yes	No	Prazosin	Yes	No
13	Prazosin	No	Yes	Placebo	No	No
17	Prazosin	No	Yes	Placebo	Yes	No
18	Prazosin	Yes	Yes	Placebo	No	Yes

Figure 2 shows the severity of AMS for the 15 subjects during phase 1. Within 4 h of altitude exposure, there was a significant increase in the incidence (Table 3) and severity of AMS. The AMS symptom severity peaked at 16 h and diminished towards sea-level values thereafter.

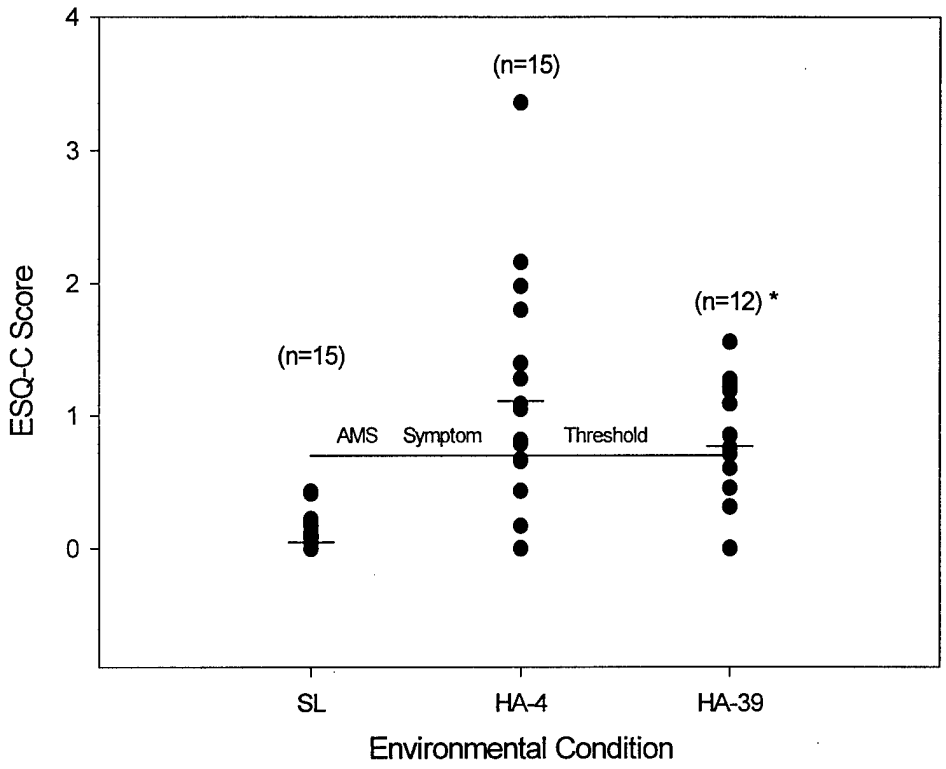
Figure 3 illustrates the range in individual ESQ-C scores of the subjects after 4 and 39 h of altitude exposure. These time periods were used in testing for possible relationships with speech production variables. Ten of the 15 subjects at the 4 h period had scores above the 0.7 threshold considered significant for AMS whereas 8 of the 12 remaining subjects at 39 h were considered ill.

Figure 2. Severity of AMS during the 48-h exposure to 4,300 m. Mean (±SE) scores were obtained during phase 1 of the study. Abscissa labels indicate environmental condition and hours of exposure.



* P < 0.001 vs. Sea Level
** P = 0.04 vs. Sea Level

Figure 3. Individual ESQ-C scores at sea level and after 4 and 39 h of exposure to 4,300 m simulated altitude. Small horizontal bars indicate mean values. Large horizontal bar represents the 0.7 threshold criteria for AMS .

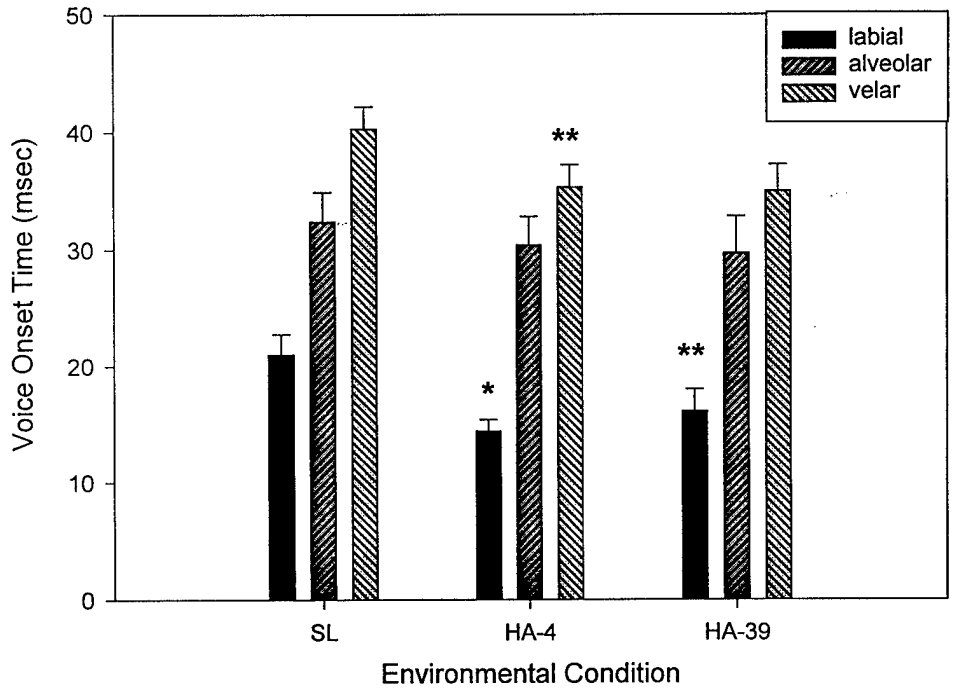


* Three subjects were withdrawn from study due to severe AMS.
Subjects with very similar scores are indicated by one symbol.

SPEECH PRODUCTION

Consonants were categorized as being voiced or unvoiced stop and as labial, alveolar, or velar (Table 2). Figure 4 shows the effects of 4 ad 39 h of exposure on the 'voiced' consonants at the three sites of articulation. VOT of the voiced-labial consonant (b) was significantly shorter after 4 h exposure (p=0.006) and 39 h (p=0.05). The VOT of the voiced-velar consonant (g) was significantly reduced only after 4 h. There was no effect on the alveolar consonants, whether voiced or unvoiced. The relative relationship between the sites of articulation were not changed during altitude exposure; i.e., labial VOTs were always shorter than alveolar, which were always shorter than velar.

Figure 4. Effect of altitude exposure on VOT of the voiced consonants (b, d, and g) representing their respective labial, alveolar, and velar locations.



* P=0.006, ** P=0.05 versus sea level

Figure 5 shows the range of individual VOT values of the labial voiced and unvoiced consonants b and p. VOTs of voiced consonants are typically in the 20 msec range while unvoiced consonants are ~40 msec or longer. Note the lower values indicated by the square symbols for the p unvoiced consonant are in the range that characterizes voiced consonants. The square symbols represent a subject of eastern European descent with English as a second language.

Figure 5. Individual VOT values for the labial consonants b and p. Small horizontal bars represent mean values.

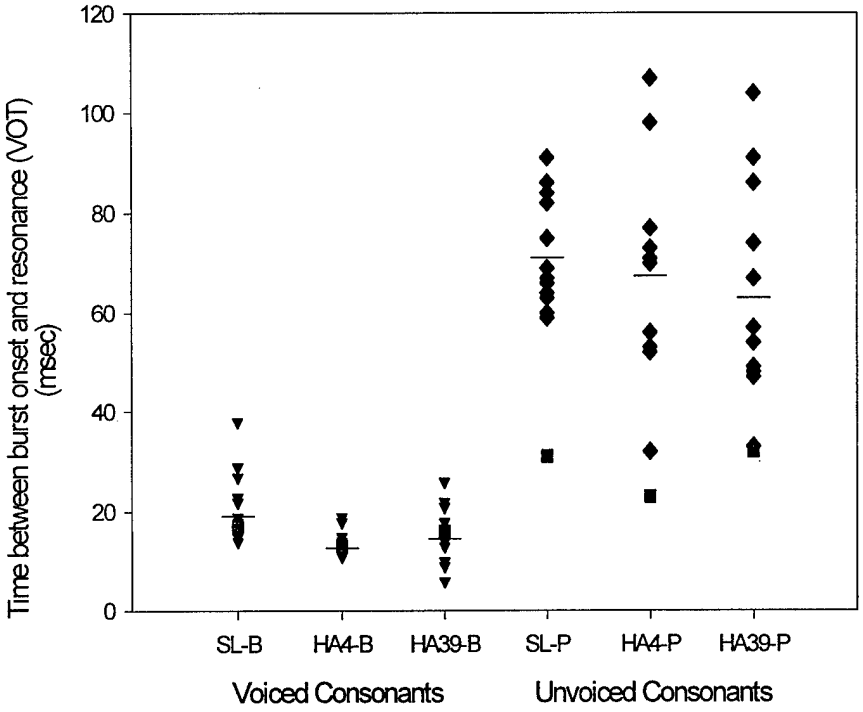
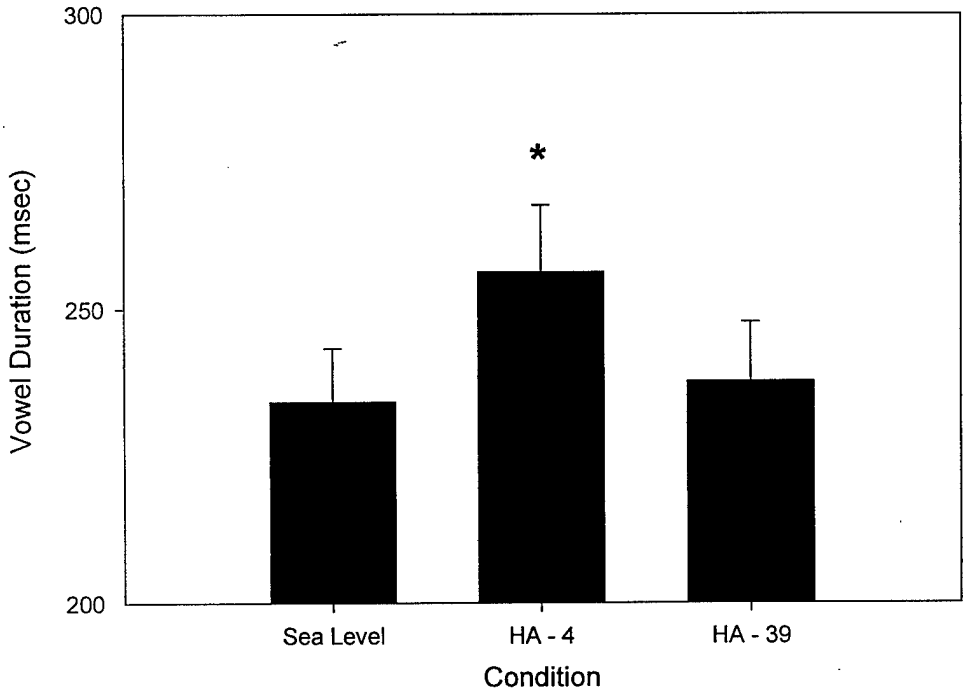


Figure 6 illustrates the effects of altitude exposure on the vowel duration. There was a significant lengthening of vowel sounds only after 4 h of exposure (p=0.001). Mean vowel duration at 4 h increased 9.4% and at 39 h increased 3.4 %.

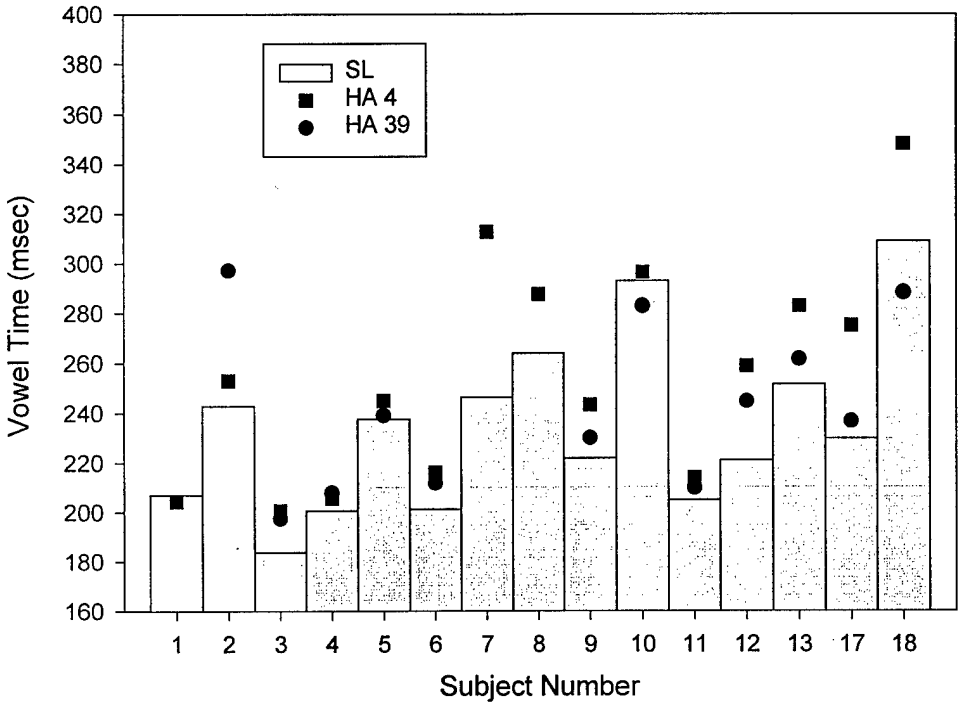
Figure 6. Effect of altitude exposure on duration of vowel sounds



* P = 0.001 compared to sea level

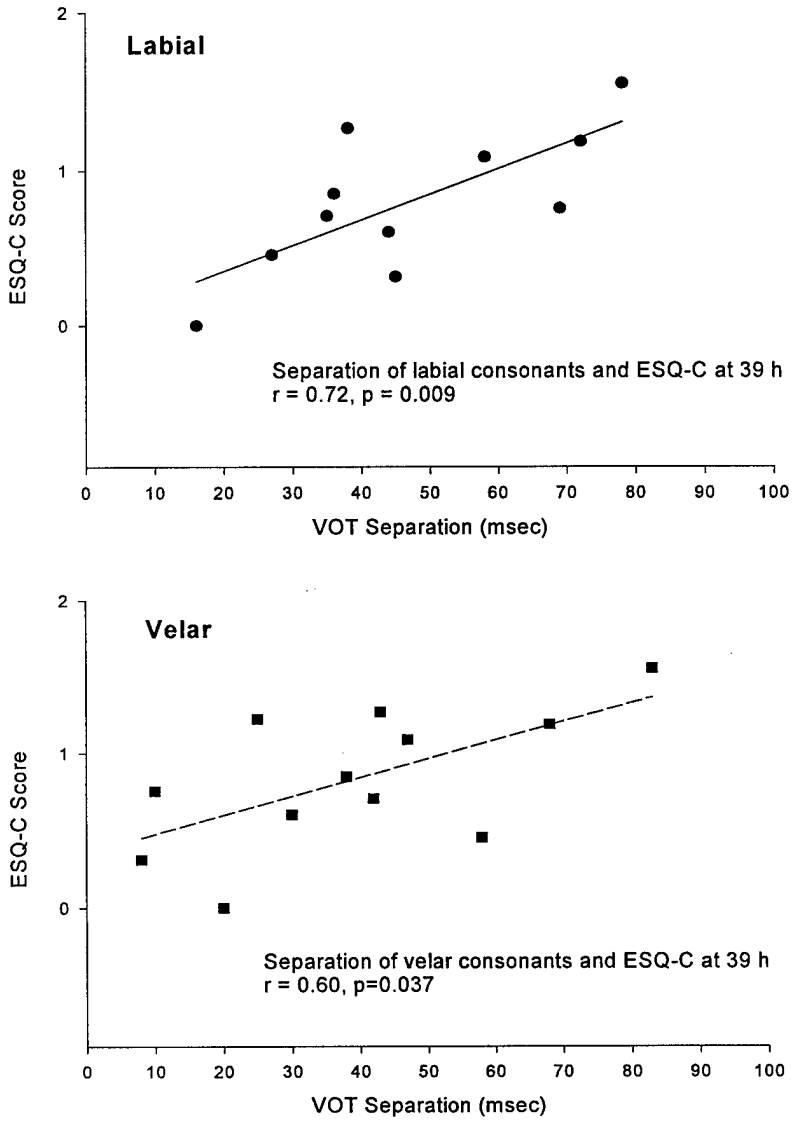
Only 1 of the 15 subjects did not increase vowel duration after 4 h of exposure (Figure 7). After 39 h, only 2 of the 12 subjects had vowel durations shorter than their initial sea-level values.

Figure 7. Effects of altitude on vowel duration by subject



Significant positive correlations were found between the minimum time differences of voiced and unvoiced consonants at the labial and velar articulation locations (39 h data) and symptoms of AMS (Figure 8). Only a trend ($p = 0.12$) was found between vowel duration and AMS severity.

Figure 8. Relationship between VOT separation and Acute Mountain Sickness



DISCUSSION

This study tested two hypotheses. The first hypothesis was that deficits in speech motor control would be evident during a 48-h exposure to 4,300 m simulated altitude. The second hypothesis is that VOT, a measure of speech production, would be affected by the presence of AMS. Our results indicate that there are components of speech production that are adversely affected by hypoxia. Namely, the voiced stop consonants b and g showed significantly decreased VOTs during simulated altitude exposure. Vowel durations also showed significant lengthening during acute exposure. Our results also indicate that VOT separation of the consonant pairs at the labial and velar locations do correlate with the severity of AMS. However, we cannot explain why VOTs of voiced consonants decreased with no change in their unvoiced counterparts, making VOT separation longer rather than shorter as has been previously observed with very high altitude exposure.

This substudy was a component of a larger multidisciplinary study testing the hypothesis that pharmacologic attenuation of α-adrenergic activity would alter the "normal" hypoxia-induced physiologic changes associated with altitude acclimatization. A double-blind, placebo-controlled, crossover design was used to test the effect of oral prazosin, an α-adrenergic blocker, on physiologic parameters indicative of acclimatization in women. Statistical analysis of the ESQ values between the two phases of the crossover revealed that subjects had higher ESQ-C scores on phase 1 of the crossover regardless of whether they were on drug or placebo. Statistical analysis also revealed that there was no significant difference between drug and placebo ESQ scores. Therefore, we felt justified in using only the phase 1 of the crossover in making our analyses for the following reasons. We obtained a good range in AMS incidence and severity.

A sufficient range of AMS was produced in these subjects with a 48-h exposure to 4,300 m. Ten of 15 subjects had significant symptoms after 4 h. Unfortunately, voice measurements were not taken at the time of peak AMS symptoms. During phase 1, three subjects were removed from the study prior to the data collection at 39 h. Unfortunately, no voice measurements were taken immediately prior to removal of these subjects from the hypobaric chamber. After 39 h, 8 of the remaining 12 subjects were still above the 0.7 illness threshold. These results are comparable with previous hypobaric chamber studies conducted at 4,300-4,570 m that are designed to induce AMS (1,16-18,21,22,24).

The rationale for attempting to discover a relationship between AMS and deficits in speech production is based on findings that there is selective hypoxic vulnerability of the brain leading to the symptoms of AMS. From histologic studies, Brierley (4) has identified areas of the brain that appear to be more vulnerable to hypoxia. Dysfunction in areas of the hippocampus, cerebellum, neocortex, and basal ganglia have possible relevance to symptoms of AMS and the direct, acute effects of hypoxia. It is also well accepted that as hypoxia becomes more severe, there is a progressive involvement of different senses and psychomotor tasks from vision-related processes to postural stability and reaction times (8). It is conceivable that speech production may be affected by hypoxia in a subtle fashion at less than severe hypoxic exposures before it becomes obvious to the speaker or the listener.

One of the advantages of determining whether disturbances in speech production exist at

altitude is the objectivity of the measurement. Questionnaires suffer from several problems that are difficult to circumvent. Important questions can be glossed over when illness is present. Having an individual with AMS in close proximity can also adversely affect a "well" individual, and vice versa, an ill individual may not report a significant symptom score when the esprit de corps of his/her colleagues is high. Motivation and consistency of administration are a concern. Lack of feedback to the subject can also have a negative impact. Regardless of these disadvantages, the questionnaire remains the standard by which the incidence and severity of AMS is currently studied, but an objective measurement that is not biased by subject or investigator would be a welcome addition to AMS measurement tools.

Speech production (i.e., VOT) is basically an unconscious process. It is not affected by complications imposed by motivation and surrounding circumstances that may affect questionnaire responses. Obtaining an objective, simple measure of AMS would simplify data collection and provide a further validation of illness severity that was based on the ESQ. Speech production, without its cognitive and associative properties, may provide the means to assess AMS severity that is above conscious control of the ill subject. The characteristics of vocalization of specific consonants and vowel duration that are measured are not usually thought about while the subject is pronouncing the words. Context on this test has no bearing.

We obtained some evidence that speech production is affected by altitude. VOTs from two (b and g) of the six consonants (b, d, g, p, t, and k) and vowel duration showed statistical changes at altitude. There was a shortening of VOT for the voiced stop labial consonant b after 4 and 39 h of exposure and for velar voiced consonant g after 4 h of exposure. Vowel duration is also increased after 4 h of exposure. Only 1 of the 15 subjects did not increase vowel duration after 4 hour, and only 2 of the remaining 12 subjects had vowel durations shorter than their sea-level values.

With respect to correlations with AMS, significant positive correlations were found with two variables: minimum VOT differences between voiced and unvoiced consonants at the labial and velar locations. The greater the VOT difference or separation, the greater was the AMS severity. These results appear to be in contrast with those previously reported by Lieberman et al. (20). Whereas they found a smaller VOT separation with increasing altitude, the results of the present study appear to be in the opposite direction. They did not measure AMS, and they possibly had confounding factors of exhaustion, dehydration, hypothermia, etc., usually encountered in a climb of Mt. Everest. A unique aspect of their study, in addition to changes they observed, was that the data were collected by radio from a site less hazardous to the investigators. If the technique proves valid, then its application to a military environment where soldiers are experiencing fatigue, hypothermia, sleep deprivation, etc., would be relatively easy. Thus, it is conceivable that valuable information could be obtained from a remote site using radio communication without endangering additional personnel.

CONCLUSIONS

In summary, this study found several objective measures of speech production that were

affected by exposure to 4,300 m simulated altitude. Voice onset timing of two of the three voiced consonants decreased with a 4-h exposure. One remained reduced after 39 h of exposure. The VOT differences between two associated pairs of voiced and unvoiced consonants were found to correlate with AMS severity. Therefore, it appears that speech production is altered in very subtle ways with exposure to 4,300 m. This alteration is not readily apparent to the subject and may be related to his/her AMS severity. The results of this study are promising, but further validation is necessary before the method can be used to assess AMS.

REFERENCES

1. Aoki, V.S. and S.M. Robinson. Body hydration and the incidence and severity of acute mountain sickness. J Appl Physiol, 31:363-367, 1971.

2. Baum, S.R., S.E. Blumstein, M.A. Naeser, and C.L. Palumbo. Temporal dimensions of consonant and vowel production: an acoustic and CT scan analysis of aphasic speech. Brain Lang, 39:33-56, 1990.

3. Bond, Z.S. and H.F. Wilson. Acquisition of the voicing contrast language-delayed and normal-speaking children. J Speech Hear Res, 23:152-161, 1980.

4. Brierley, J.B.. Cerebral hypoxia. In: Greenfield's Neuropathology, W. Blackwood and J. Corsellis (Eds.). Yearbook Medical Publishers, Chicago, 1976, pp. 43-85.

5. Catts, H.W. and P.J. Jensen. Speech timing of phonologically disordered children: voicing contrast of initial and final stop consonants. J Speech Hear Res, 26:501-510, 1983.

6. Cymerman, A. and P.B. Rock. Medical problems in high mountain environments: A handbook for medical officers. USARIEM Technical Note TN 94-2, February 1994.

7. Eilers, R.E., P.A. Morse, W.J. Gavin, and D.K. Oller. Discrimination of voice onset time in infancy. J Acoust Soc Am, 70:955-965, 1981.

8. Fulco, C.S. and A. Cymerman. Human performance and acute hypoxia. In: Human Performance Physiology and Environmental Medicine at Terrestrial Extremes, K.B. Pandolf, M.N. Sawka, and R.R. Golzalez (Eds.). Benchmark Press, Indianapolis, 1988, pp. 467-495.

9. Grossman, M., S. Carvell, S. Gollomp, M.B. Stern, G. Vernon, and H.I. Hurtig. Sentence comprehension and praxis deficits in Parkinson's disease. Neurology, 41:1620-1626, 1991.

10. Hackett, P.H., D. Rennie, R.F. Grover, and J.T. Reeves. Acute mountain sickness and the edemas of high altitude: A common pathogenesis? Respir Physiol, 46:383-390, 1981.

11. Hackett, P.H. and R.C. Roach. High-altitude medicine. In: Wilderness Medicine: Management of Wilderness and Environmental Emergencies, P.S. Auerbach (Ed.). Mosby-Year Book, Inc., St. Louis, MO, 1995, pp. 1-37 .

12. Hackett, P.H., P.R. Yarnell, R. Hill, K. Reynard, J. Heit, and J. McCormick. High-altitude cerebral edema evaluated with magnetic resonance imaging: clinical correlation and pathophysiology. JAMA, 280:1920-1925, 1998.

13. Hertrich, I. and H. Ackermann. Acoustic analysis of speech timing in Huntington's disease. Brain Lang, 47:182-196, 1994.

14. Hultgren, H.. High Altitude Medicine. Hultgren Publications, Stanford, 1997.

15. Johnson, T.S. and P.B. Rock. Acute mountain sickness. N Engl J Med, 319:841-845, 1988.

16. Johnson, T.S., P.B. Rock, C.S. Fulco, L.A. Trad, R.F. Spark, and J.T. Maher. Prevention of acute mountain sickness by dexamethasone. N Engl J Med, 310:683-686, 1984.

17. King, A.B. and S.M. Robinson. Vascular headache of acute mountain sickness. Aerospace Med, 43:849-851, 1972.

18. Larsen, R.F., P.B. Rock, C.S. Fulco, B. Edelman, A.J. Young, and A. Cymerman. Effect of spironolactone on acute mountain sickness. Aviat Space Environ Med, 57:543-547, 1986.

19. Lieberman, P., E. Kako, J. Friedman, G. Tajchman, L.S. Feldman, and E.B. Jiminez. Speech production, syntax comprehension, and cognitive deficits in Parkinson's disease. Brain Lang, 43:169-189, 1992.

20. Lieberman, P., A. Protopapas, and B.G. Kanki. Speech production and cognitive deficits on Mt. Everest. Aviat Space Environ Med, 66:857-864, 1995.

21. Meehan, R.T., A. Cymerman, P. Rock, C.S. Fulco, J. Hoffman, C. Abernathy, S. Needleman, and J.T. Maher. The effect of naproxen on acute mountain sickness and vascular responses to hypoxia. Am J Med Sci, 292:15-20, 1986.

22. Muza, S.R., T. Lyons, P.B. Rock, C.S. Fulco, B.A. Beidleman, W.L. Smith, I.A. Morocz, G.P. Zientera, and A. Cymerman. Acute Mountain Sickness: Relationship to brain volume and effect of oral glycerol prophylaxis. USARIEM Technical Report T98-20, June 1998.

23. Paul-Brown, D. and G.H. Yeni-Komshian. Temporal changes in word revisions by children and adults. J Speech Hear Res, 31:630-639, 1988.

24. Rock, P.B., T.S. Johnson, R.F. Larsen, C.S. Fulco, L.A. Trad, and A. Cymerman. Dexamethasone as prophylaxis for acute mountain sickness. Effect of dose level. Chest, 95:568-573, 1989.

25. Sampson, J.B., A. Cymerman, R.L. Burse, J.T. Maher, and P.B. Rock. Procedures for the measurement of acute mountain sickness. Aviat Space Environ Med, 54:1063-1073, 1983.

26. Singh, I., P.K. Khanna, M.C. Srivastava, M. Lal, S.B. Roy, and C.S.V. Subramanyam. Acute mountain sickness. N Engl J Med, 280:175-184, 1969.

27. Sutton, J.R. and N. Lassen. Pathophysiology of acute mountain sickness and high altitude pulmonary oedema: an hypothesis. Bull Eur Physiopath Respir, 15:1045-1052, 1979.